UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,938	04/13/2006	Jess G. Thoene	TUL5AUSA	7083

270 7590 07/09/2008

HOWSON AND HOWSON
SUITE 210
501 OFFICE CENTER DRIVE
FT WASHINGTON, PA 19034

EXAMINER	
GUDIBANDE, SATYANARAYAN R	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
07/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,938	THOENE, JESS G.	
	Examiner	Art Unit	
	SATYANARAYANA R. GUDIBANDE	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,12,13,15,28,30 and 32-36* is/are pending in the application.

4a) Of the above claim(s) *2,3 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,12,15,28,30 and 32-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/1/07,6/12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of group I (claims 1(in part), 2, 3, 4(in part), 12, 13 and 28, 30 and 32), and election of cysteine dimethyl ester (CDME), breast cancer as the elected species of cancer and radiation as the species of cytotoxic agent in the reply filed on 4/10/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

A search for the elected species CDME indicated that it is not free of art. The art found has been applied to the rejections below.

Claims 1-4, 12, 13, 15, 28, 30, 32-36 are pending.

Claims 33-36 are new claims.

Claims 5-11, 14, 16-27, 29 and 31 are canceled.

Claims 2, 3 and 13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/10/08.

Claims 2, 3 and 13 have been withdrawn from further consideration as being drawn to non-elected species. Since the art was found on the elected species CDME, the compounds

represented by structure as shown in claims 2 and 3 (with Xm as recited), represents a structure other than the elected species CDME and claim 13 recite a cytotoxic agent which is an apoptotic compound or a chemotherapeutic agent which is different from radiation (elected species). Hence claims 2, 3 and 13 have been withdrawn from further consideration.

Claims 1, 4, 12, 15, 28, 30 and 32-36 are examined on the merit.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites a limitation "upon exposure to a susceptible cell increases the cell's intralysosomal cystine level above 0.5 nmol/mg cell protein". It is unclear from the claim as recited whether the cystine level in the cell increases above 0.5 nmol/mg in the lysosome or the cystine concentration in lysosomal protein increases to greater than 0.5 nmol/mg.

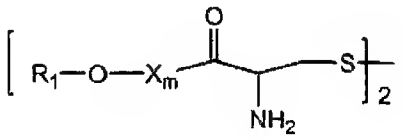
Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 12, 15, 28, 32, 35 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims of the instant invention claims a pharmaceutical composition useful for the treatment of cancer comprising a compound of the formula,



Wherein 'X' is any naturally or non-naturally occurring amino acid and 'm' is an integer of 0-20 or a pharmaceutically acceptable salt in a pharmaceutically acceptable carrier.

The claim as recited claims a product and a method of treating any and all forms of "cancer" with innumerable known and unknown compounds represented by the above depicted formula. The formula shown above encompass any and all cystine compounds wherein the variable "X" is represented by peptides of length 0 to 20 units composed of not only 20 naturally occurring amino acids but any and all known and unknown non-naturally occurring amino acids of known and unknown structural features. Over and above the terminal ends are esters of substitutes or unsubstituted alkyl chains of 1-10 carbon atoms. The specification has support for the use of the elected species CDME in in vitro studies of breast cancer cell lines (example 4), toxicity study in example 5 and in vivo study of breast cancer in nude mice.

The MPEP clearly states that the purpose of the written description is to ensure that the inventor had possession of invention as of the filing date of the application, of the subject matter later claimed by him. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997). The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the application. These include, "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed invention is sufficient" MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In_*Regents of the University of California v. Eli Lilly & Co.*, the court stated: "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. _*Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations

other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

The instant specification as afore-illustrated has shown support for the study of elected species CDME in breast tumor cell lines and in vivo studies in nude mice. The specification as disclosed does not adequately support the instant invention as recited in the claims to commensurate with the scope of the claims. The specification does not show adequate support in terms of other compounds commensurate with the vast scope of the claim as recited that encompasses peptides of known and unknown structural features comprising other natural and unnatural amino acids with the exception of the elected species that recite cysteine. The claims as

recited as mentioned earlier encompasses innumerable compounds. Even with only 20 natural amino acids if m=20, the number of compounds that the formula as depicted above represents 20^{20} molecules where in the position of each amino acid at position can be any of the 20 naturally occurring residues. Further inclusion of any and all known and unknown non-natural amino acids and inclusion of 'R1" variable as a substituted or unsubstituted alkyl of 1-10 carbon atoms, introduces even more complexity to the molecule. Mere disclosure of a formula without disclosing representative specific examples in terms of complete or core structural features does not lend adequate written description. The cited prior art reference of Pisoni, 1992, Somatic cell and molecular genetics, 18, 1-6 discloses the use of CDME in the study of cytotoxicity in human fibroblasts.

Therefore, the claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

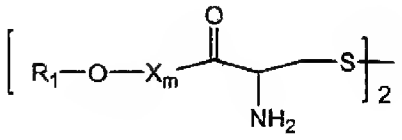
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 15, 12, 33 and 36 rejected under 35 U.S.C. 102(b) as being anticipated by Kitazawa, 2002, FEBS Letters, 526, 106-110.

The claims of the instant invention claims a pharmaceutical composition useful for the treatment of cancer comprising a compound of the formula,



Wherein 'X' is any naturally or non-naturally occurring amino acid and 'm' is an integer of 0-20 or a pharmaceutically acceptable salt in a pharmaceutically acceptable carrier.

The reference of Kitazawa discloses N,N'-diacetyl-L-cystine dimethylester (DACDM) which is N-acetyl salt of CDME in the intracellular redox regulation of UV-induced NF-kB activation (Title and abstract). The N-acetyl salt of CDME meets the structural limitations of formula recited in claims 1 and claim 4. The reference teaches that UV irradiation induces NF-kB activation in human skin and regulates inflammatory cytokine genes such as IL-1beta and TNF-alpha (Introduction, page 106, column 1). The reference teaches cystine derivative DACDM and NAC were tested in cell culture medium. This meets the limitation for the pharmaceutical composition of DACDM and hence meets the limitation of instant claims 1, 4 (in part). The limitation "for treatment of cancer" is an intended use and does not provide limitations as to any structural element necessary in the compound or composition.

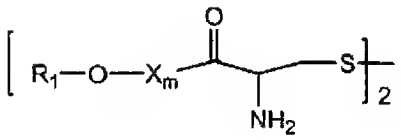
In the instant case, the claims are drawn to a pharmaceutical composition comprising the formula shown above and in instant claim 1 with the elected species being CDME. The cited reference teaches DACDM in cell culture medium and hence it is inherent that it can be used for treating cancer cells including breast cancer cells. Hence reads on instant claims 1 and 33. The reference also teaches concentration of DACDM of 0.001 to 0.1 mM in culture medium. This

enhanced the glutathione levels in the range 17.6-20.3 mmol/g of protein (table 2 on page 108) and glutathione peptide comprises of amino acid cysteine and hence reads on instant claim 15. The cells were treated with UV radiation in the presence of the DACDM (page 107, section 2.4) and hence reads on instant claim 35 and 36.

Therefore, the reference of Kitazawa anticipates instant invention.

Claims 1, 4, 15, 28, 30, 33 and 34 rejected under 35 U.S.C. 102(b) as being anticipated by Pisoni, 1992, Somatic cell and molecular genetics, 18, 1-6.

The claims of the instant invention claims a pharmaceutical composition useful for the treatment of cancer comprising a compound of the formula,



Wherein 'X' is any naturally or non-naturally occurring amino acid and 'm' is an integer of 0-20 or a pharmaceutically acceptable salt in a pharmaceutically acceptable carrier.

The reference of Pisoni discloses the elected species CDME in culture medium containing 10% fetal bovine serum, pH 7.2, sterilized via ultra filtration with 0.22 micron filter (page 2, column 2, paragraph 1). This meets the limitation for the pharmaceutical composition of CDME and hence meets the limitation of instant claims 1, 4. The limitation "for treatment of cancer" is an intended use. In the instant case, the claims are drawn to a pharmaceutical

composition comprising the formula shown above and in instant claim 1 with the elected species being CDME. The cited reference teaches CDME in cell culture medium and hence it is inherent that it can be used for treating cancer cells. Hence reads on instant claims 1, 4 and 33.

The reference also teaches concentration of CDME of 20 mM in culture medium. This enhanced the cysteine content levels in the range 2-8 nmol cysteine/million cells (Fig. 1 on page 3) and hence reads on instant claim 15.

The reference of Pisoni discloses that CDME is prone to hydrolysis in aqueous solutions and hence CDME solutions are prepared fresh on the day of administration indicating that the compound be dispensed in appropriate quantity in powdered (dosage) form convenient to prepare a solution in culture medium with pH adjusted to 7.2 (page 2, column 2, paragraph 1). This reads on instant claims 28 and 30 that recite the kit comprising CDME. Since the composition can be used for fibroblast cells, it can be used for treating any cells including cancer cells specifically breast cancer cells and hence reads on instant claims 33 and 34.

Therefore, the reference of Pisoni anticipates instant invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Satyanarayana R Gudibande/
Examiner, Art Unit 1654

/Andrew D Kosar/
Primary Examiner, Art Unit 1654